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The Gaseous Environment and Temperature Regulation

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Studies have been continued on the effects of carbon dioxide and hypoxia on mechanisms involved in temperature regulation. These effects have also been compared to those of other agents or factors altering thermoregulation.

A method for continuous recording of sweating activity has been further developed in this laboratory. The method consists of constant flow of dry air over selected skin areas and past one or more electric hygrometer sensing elements. The system has rapid response time and cyclic sweating activity may be recorded.

Cyclic sweating activity has been studied during 6% carbon dioxide inhalation in men exposed between 38°C and 44°C. Initially carbon dioxide augmented sweating rate which then subsided to levels above control levels. The measurement of tympanic membrane temperature yielded no evidence that the carbon dioxide effect is due to resetting of hypothalamic thermal set points. The failure of carbon dioxide to increase cyclic rate (cycles/min) and the blocking of the augmentation under a limb occlusion suggest that the carbon effect may be local.

Exercise by men exposed at 40°C produced an immediate increased sweating rate with increased cyclic rate and cyclic magnitude. This response occurred prior to any increases of tympanic membrane temperatures, rectal temperatures, and skin temperatures.

Effects of carbon dioxide and hypoxia have been compared to the effect of tranquilizers on temperature regulation in the rat.

Objective of Project

The major objective of this project has been to determine the effects of oxygen deficiency and carbon dioxide excess upon physiological mechanisms utilized for body temperature regulation. An effort has also been made to compare these effects to those of other factors altering temperature regulation.

Part I. Continuous recording of sweating rate by resistance hygrometry. (Reference 5)

A method for continuous recording of sweating by the use of resistance hygrometry has been developed in this laboratory. The essentials of this method were described in the annual report of 1962 and in reference no. 5. A more satisfactory method of relative humidity (RH) control of the supply air has been developed in the past year. Air from the pressure regulated building supply is passed through saturated Drierite, which acts as a constant humidity solution and eliminates any minor relative humidity changes. Fine RH adjustment may then be obtained by the use of a three way system in which a certain portion of the supply air may be either dried or humidified. Thus the pre-test baseline may be set at the desired humidity level which in our experiments is usually 8% RH.

The incoming air passes through calibrated flowmeters and then through small cups (area = 7 cm^2) mounted over selected skin areas. The effluent air enters a thermostatically controlled chamber at 45°C, through a heat exchanger and then blows over the sensing elements. By the use of the heated chamber RH changes are always monitored at the same constant temperature. Thus the calibration procedure will hold for all ranges of experimental ambient temperature.

Calibration of the instrument is done under conditions as close to the actual experimental conditions as possible. The most satisfactory method of calibration has been to place the skin cups directly over a combination of one, two or three small plastic capsules having holes of different sizes drilled into them. The capsules are stuffed with cotton and are water filled to present a constant area for evaporation which is recorded for a known time period at an air flow rate used in the experiments (usually 1.8 l/min.). The capsule weight loss, to the nearest mg, is then compared to the recorded deflection and a calibration plot of reading versus mg. of water evaporated/minute is obtained.

Part II. Cyclic Sweating Activity

A. Studies have been continued on sweating cycles under a variety of conditions. Albert and Palmes (J. Appl. Physiol. 4: 208, 1951) observed that the cycling is parallel from different body areas and concluded that these cycles were under the control of the central nervous system. This observation has been repeated many times by us, and with the same conclusion. The cyclic activity may be due to rhythmic contraction of the myoepithelial elements of the sweat gland duct.

The cyclic rate appears to vary from individual to individual. However, in all individuals the cyclic rate increased with temperature from 0/min at cooler temperatures to around 20/min at higher temperatures. A fair correlation of cyclic rate and total sweating may also be obtained. However, we have not recorded cyclic rates over 20/min even though the high air flow provides good resolution of cycles at lower cyclic rates. Either the response time of the recording system is insufficient, or perhaps the cycles become merged at the higher rates.

B. Occlusion Experiments.

Arterial occlusion results in a steady decline of total sweating activity. The cyclic rate (cycles/min) may remain unchanged with the occluded limb showing the identical cyclic rate as unoccluded areas. The magnitude of the cycles continuously declines and sweating ceases between 10 and 20 minutes of occlusion. The pattern fits with the concept that activity at the gland level fails even though the central influence is still acting.

Venous occlusion of the limbs had little effect on magnitude or cyclic rate. Occluding cuff pressures ranged from 10 to 90 mm Hg with only a slight decrement of sweating at the highest pressure. These observations are of interest as Gold has concluded that "cessation of sweating is a result of rising venous pressure" in the development of heat stroke (J.A.M.A., 173: 1173, 1960.) We have concluded that uncomplicated increases in peripheral venous pressure have little effect upon sweating rate. Studies are being continued on the effects of central venous pressure changes on sweating rate, utilizing various respiratory manouvers and tilt table procedures.

C. The Effects of Carbon Dioxide Inhalation on Sweating.(References (References 11, 14)

Increased sweating during inhalation of carbon dioxide and air mixtures has been commonly observed. Studies on the nature of this response have been in progress in this laboratory for the past 3 years. The results are presented in last year's annual report and in references 11 and 14. Experiments in the past year have consisted of attempts to elucidate mechanisms of action.

The cyclic rate (cycles/min) was increased slightly in some subjects sitting in a warm room and inhaling a mixture of 6% carbon dioxide and air. However, an increase in cyclic rate does not always occur, yet an initial increase in the magnitude of sweating was a consistent finding during the inhalation. If cyclic rate is a phenomenon under central control and if carbon dioxide effects were upon central mechanisms an increase in cyclic rate could be expected.

After 6 to 10 minutes of inhalation of the 6% carbon dioxide a definite decrease in cyclic rate occurred as well as a decrease in magnitude. If the hypothesis of a central origin is correct then perhaps this decrease in cyclic rate was because sensory information being received by the central

nervous system indicated cooling as a result of the initially augmented sweating. Thus the efferent sweating outflow is decreased. Following carbon dioxide inhalation cyclic activity may halt completely.

The decline in sweating after the increase on carbon dioxide and the further decline in the recovery period are thus considered to be central nervous system responses because of the marked change in cyclic rate. Evidence for central mediation of the initial sweating rate increase on carbon dioxide inhalation was not as clear and another approach has been made to this problem. The subjects during a two hour exposure at 43°C breathed the 6% carbon dioxide mixture at selected time periods. Just prior to the inhalation period the arterial blood supply to one limb was occluded. Although the occluded limb could still show cyclic sweating activity the carbon dioxide induced increase was never seen. This yields partial evidence that the carbon dioxide increase of sweating may be mediated locally. The major criticism of this approach is that the environment under an occlusion would hardly be considered normal, as carbon dioxide would be accumulating. Inspite of this the consistent block by occlusion must be given major consideration in attempting to explain the carbon dioxide response.

The characteristic response on carbon dioxide inhalation is analogous to that which would occur if the thermostat of a cooling system were readjusted to a lower thermal "set point". Greatly increased cooling activity would be required to reach the new set point. Cooling activity could then decline, but higher than normal activity would be required because now the temperature gradient has been increased. When the thermostat is reset back up to normal, no cooling activity would be required until the raised set point level had again been reached. This is similar to the characteristic sweating curve obtained during inhalation of carbon dioxide and in the recovery period. Attempts to verify "resetting" as the mechanism were made by recording continuously the temperature of the tympanic membrane by the method described by Benzinger (Proc. Nat. Acad. Sci. 45: 645, 1959). The correlation of sweating rate with "intracranial temperature" was no better than that with rectal temperature under these circumstances. Such experiments suggest that either no "resetting" occurs, or that the tympanic membrane temperature is distinctly different from that at the hypothalamic temperature detectors. The best correlations of sweating activity were with skin temperature.

D. Exercise Stimulation of Sweating. *

The influence of muscular exertion on cyclic patterns was studied by the previously described method of resistance hygrometry. Particular attention has been given to the rate of onset of sweating at different work rates and at different ambient temperatures. At ambient temperatures high enough to produce sweating in a resting subject an immediate increase in sweating rate occurred at the start of work consisting of either forearm flexion, a modified step test, or pedaling a bicycle ergometer. The sweating rate increase was due to both an increase in magnitude and an increase in cyclic rate and occurred in both active and inactive areas. The promptness of the sweating response suggested a reflex mechanism rather

* Abstract of a paper to be presented by W. van Beaumont at the Annual Meeting of the American College of Sports Medicine.

than an effect of increased body heat stores or brain temperature. Rectal temperatures and tympanic membrane temperatures which were continuously recorded showed increases too late to explain the sweating increase. The reflex mechanisms involved could originate in some type of deep body receptor or from irradiation of descending motor impulses. The response is definitely related to thermal factors as a delay was seen at cooler ambient temperatures. An interesting pattern was seen at warmer temperatures (40.5) with the lightest work loads used. After the initial increase of sweating at the start of exercise a marked decline in sweat rate occurred. This again may indicate a reflex origin of sweating stimulation.

Part III. Animal Experiments with J. Kollias

Efforts have been made in this laboratory to determine the effects of hypoxia, carbon dioxide and various thermolytic drugs on physical and chemical mechanisms of temperature regulation in the rat. Measurements of a central temperature (colonic), skin temperatures and peripheral blood flow (venous occlusion plethysmography) were made for evaluation of alterations in physical mechanisms. Simultaneous measurements of oxygen consumption permitted evaluation of any alteration of chemical mechanisms.

A. Hypoxia and Temperature Regulation in the Laboratory Rat. (Reference 15)

The primary effect of hypoxia in lowering the body temperature of the rat exposed to an ambient temperature of 23°C was depression of metabolic heat production. Blood flow to the tail increased slightly and tail skin temperature increased slightly and transiently upon inhalation of 10% oxygen in nitrogen. The increased surface temperature was neither great enough nor prolonged enough to explain the body cooling, as the surface temperatures soon dropped below those of rats in control exposures. The surface to ambient temperature gradient was actually reduced and thus the increased cooling could not be attributed to alteration of physical regulation.

B. Comparative Effects of Tranquilizers on Temperature Regulation. (References 12, 16, 17, 18)

The effects of three tranquilizers on chemical and physical mechanisms of temperature regulation have been investigated in the rat. All drugs were administered i.p. at a dose of 25 mg/Kg. At 23 C°chlorpromazine (Thorazine) and 2-chloro-9-(3-dimethylaminopropylidene) thioxanthene (Taractan) similarly depressed colonic temperature and metabolism. Loss of physical regulation was evidenced by high skin temperatures with both drugs and increased tail blood flow. Although chlordiazepoxide (Librium) depressed metabolism, colonic cooling was very slight because physical regulation was not altered. At 34°C survival time of controls was 154 min., Thorazine 112 min., Librium 181 min., Taractan 190 min. The decreased tolerance to heat with Thorazine is attributed to decreased peripheral blood flow as evidenced by tail blood flow studies and not to a change in lethal temperature. Skin temperatures of Thorazine treated

rats remained below that of control animals, but colonic temperatures increased at a faster rate. Increased heat tolerance of Librium and Taractan treated animals may be attributed to decreased metabolism and/or the muscle relaxant properties of these drugs.

C. Effects of Carbon Dioxide on Heat Tolerance of the Rat. (Reference 21)

Of many agents studied the most effective in increasing survival of the rat in the heat was 6% carbon dioxide. At a chamber temperature of 35°C control rats in a restrained position had a mean survival time of 154 minutes while all those breathing 6% carbon dioxide lasted throughout the 240 minute exposure. Part of the increased tolerance was due to the forced increase of respiratory heat loss by carbon dioxide. When the air, or carbon dioxide-air mixture entering the chamber was first saturated with water vapor then the differences in survival time tended to disappear. The cause of death in carbon dioxide treated rats and control rats appeared to be different. Autopsy findings in control rats killed by heat stroke indicated greatly enlarged right ventricles and bright red lungs. Histological observations revealed that the lung capillaries were greatly engorged with blood and some hemorrhage into the alveoli were present. The carbon dioxide treated rats did not have the greatly enlarged right ventricle and the lungs showed a definite pallor. The alveolar walls appeared stretched and had given away in some areas so that two alveoli appeared as one. Control rats may have died with left ventricular failure while carbon dioxide treated rats did not. Central venous pressure and arterial pressure measurements are currently being undertaken in this type of experiment.

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